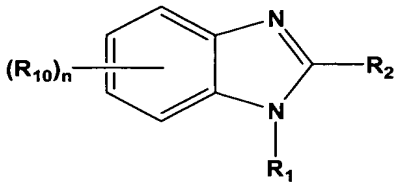
Amendments to the Claims

This listing of claims will replace all prior versions, and listings of claims in the application.

1. (Currently amended) A compound having the Formula I:

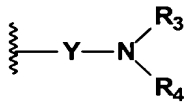


(I)

or a pharmaceutically acceptable salt, or solvate thereof, wherein:

R_1 is selected from the group consisting of:

(i)



where

Y is an optionally substituted C_{2-6} alkylene, and

R_3 and R_4 ~~are the same or different and are selected from hydrogen, alkyl, or aryl, or R_3 and R_4~~ together with the nitrogen to which they are attached form a ring having 4 or 5 carbon atoms, which ring optionally contains 1 or 2 additional heteroatoms independently selected from oxygen and NR_5, where R_5 is hydrogen or alkyl, or said ring is optionally substituted with an alkyl or aryl moiety;

~~(ii) pyridylalkyl;~~ and

~~(iii)~~ (ii) piperidin-4-ylalkyl, optionally substituted by alkyl, aryl or aralkyl;

R_2 is selected from the group consisting of:

(i) optionally substituted phenoxyphenyl;

(ii) optionally substituted benzyloxyphenyl;

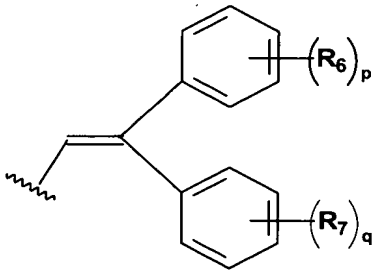
(iii) optionally substituted phenylthiophenyl;

(iv) optionally substituted benzylthiophenyl;

(v) optionally substituted phenylaminophenyl;

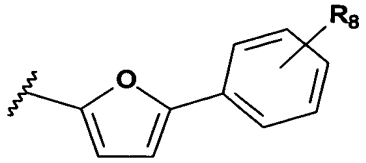
(vi) optionally substituted benzylaminophenyl;

(vii)



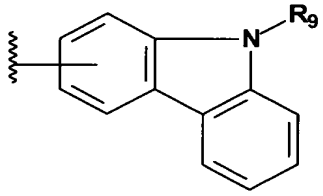
wherein R_6 and R_7 are independently halogen, alkyl, alkoxy or haloalkyl; and p and q are integers from 0 to 4;

(viii)



wherein R_8 is hydrogen, halogen, alkyl or alkoxy;

(ix)



wherein R_9 is hydrogen or alkyl; and

(x) naphthalyl;

R_{10} is selected from halogen, hydroxy, alkyl, alkoxy and alkoxyalkyl, wherein any alkyl moiety of R_{10} can be optionally substituted by one or more of halogen or hydroxy; and

n is an integer from 0 to 4, where when n is 0, R_{10} is absent and the benzene ring of the benzimidazole compound has four hydrogen atoms attached thereto, and when R_{10} is present, R_{10} replaces one or more of the available hydrogen atoms on the benzene ring of the benzimidazole compound.

2. (Original) The compound according to claim 1, wherein R_1 is $-Y-NR_3R_4$ and Y is ethylene or propylene.

3. (Original) The compound according to claim 1, wherein:

R_2 is optionally substituted phenoxyphenyl or optionally substituted benzyloxyphenyl; R_1 is $-Y-NR_3R_4$; R_3 and R_4 together with the nitrogen to which they are attached form a ring having 4 or 5 carbon atoms; and Y is an optionally substituted C_{2-6} alkylene chain.

4. (Currently amended) The compound according to claim 3, wherein R_3 and R_4 together with the nitrogen to which they are attached form a ring having 5 carbon atoms; and R_1 is $-Y-NR_3R_4$; wherein Y is an optionally substituted C_{2-6} alkylene chain.

5. (Currently amended) The compound according to claim 3, wherein R_3 and R_4 together with the nitrogen to which they are attached form a ring having 4 carbon atoms; and R_1 is $-Y-NR_3R_4$; wherein Y is an optionally substituted C_{2-6} alkylene chain.

6. (Original) The compound according to claim 5, wherein R_1 is 2-piperidin-1-ylethyl.

7. (Currently amended) The compound according to claim 1, wherein:

R_2 is optionally substituted phenoxyphenyl or optionally substituted benzyloxyphenyl; R_1 is $-Y-NR_3R_4$~~; R_3 and R_4 are independently hydrogen, alkyl or aryl~~; and Y is an optionally substituted C_{2-6} alkylene chain.

8. (Original) The compound according to claim 1, wherein R_2 is an optionally substituted phenoxyphenyl.

9. (Original) The compound according to claim 1, wherein R_2 is an optionally substituted benzyloxyphenyl.

10. (Original) The compound according to claim 1, wherein when R_2 is phenoxyphenyl or benzyloxyphenyl, and R_2 is attached to benzimidazole at the 3- or 4-position of the phenyl component of the phenoxyphenyl or the benzyloxyphenyl.

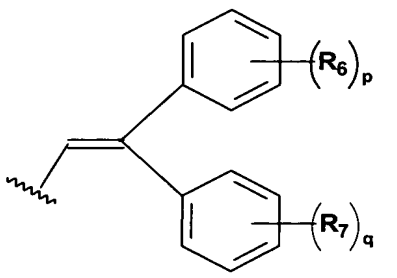
11. (Original) The compound according to claim 9, wherein R_1 is $-Y-NR_3R_4$; Y is an optionally substituted C_{2-6} alkylene and R_3 and R_4 together with the nitrogen to which they are attached form a ring having 4 or 5 carbon atoms.

12. (Original) The compound according to claim 10, wherein R_1 is $-Y-NR_3R_4$; Y is an optionally substituted C_{2-6} alkylene and R_3 and R_4 together with the nitrogen to which they are attached form a ring having 4 or 5 carbon atoms.

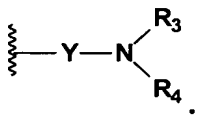
13. (Canceled)

14. (Canceled)

15. (Original) The compound according to claim 1, wherein R_2 is



16. (Original) The compound according to claim 15, wherein R_1 is

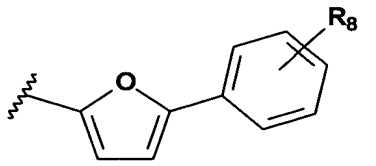


17. (Canceled)

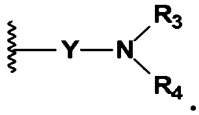
18. (Original) The compound according to claim 16, wherein Y is an optionally substituted C_{2-6} alkylene, and R_3 and R_4 together with the nitrogen to which they are attached form a ring having 4 to 5 carbon atoms, which is optionally substituted with an alkyl or aryl moiety.

19. (Original) The compound according to claim 18, wherein said ring optionally contains 1 or 2 additional heteroatoms independently selected from oxygen and NR_5, where R_5 is hydrogen or alkyl.

20. (Original) The compound according to claim 1, wherein R_2 is



21. (Original) The compound according to claim 20, wherein R_1 is

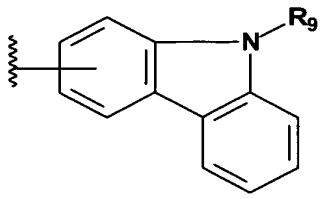


22. (Canceled)

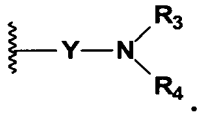
23. (Original) The compound according to claim 21, wherein Y is an optionally substituted C_{2-6} alkylene, and R_3 and R_4 together with the nitrogen to which they are attached form a ring having 4 to 5 carbon atoms, which is optionally substituted with an alkyl or aryl moiety.

24. (Original) The compound according to claim 23, wherein said ring optionally contains 1 or 2 additional heteroatoms independently selected from oxygen and NR_5, where R_5 is hydrogen or alkyl.

25. (Original) The compound according to claim 1, wherein R_2 is



26. (Original) The compound according to claim 25, wherein R_1 is



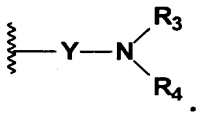
27. (Canceled)

28. (Original) The compound according to claim 26, wherein Y is an optionally substituted C_{2-6} alkylene, and R_3 and R_4 together with the nitrogen to which they are attached form a ring having 4 to 5 carbon atoms, optionally substituted with an alkyl or aryl moiety.

29. (Original) The compound according to claim 28, wherein said ring optionally contains 1 or 2 additional heteroatoms independently selected from oxygen and NR_5, where R_5 is hydrogen or alkyl.

30. (Original) The compound according to claim 1, wherein R_2 is naphthalyl.

31. (Original) The compound according to claim 30, wherein R_1 is



32. (Canceled)

33. (Currently amended) The compound according to claim ~~31~~ 30, wherein Y is an optionally substituted C_{2-6} alkylene, and R_3 and R_4 together with the nitrogen to which they are attached form a ring having 4 to 5 carbon atoms, which is optionally substituted with an alkyl or aryl moiety.

34. (Original) The compound according to claim 33, wherein said ring optionally contains 1 or 2 additional heteroatoms independently selected from oxygen and NR_5, where R_5 is hydrogen or alkyl.

35. (Original) The compound according to claim 1, wherein said compound is selected from the group consisting of:

3-(2-piperidinylethyl)-2-(4-phenoxyphenyl) benzimidazole;
3-(2-piperidinylethyl)-2-(3-(4-tert-butylphenoxy)phenyl) benzimidazole;
3-(2-piperidinylethyl)-2-(3-(3,4-dichlorophenoxy)phenyl) benzimidazole;
3-(2-piperidinylethyl)-2-(2,2-diphenylethenyl) benzimidazole;
3-(2-piperidinylethyl)-2-(3-phenoxyphenyl) benzimidazole;
3-(2-piperidinylethyl)-2-(3-(3-trifluromethylphenoxy)phenyl) benzimidazole;
3-(2-piperidinylethyl)-2-(*N*-ethyl-3-carbazolyl) benzimidazole;
3-(2-piperidinylethyl)-2-(3-benzyloxyphenyl) benzimidazole; and
3-(2-piperidinylethyl)-2-(4-(4-fluorophenoxy)phenyl) benzimidazole.

36. (Original) A pharmaceutical composition, comprising the compound of claim 1 and a pharmaceutically acceptable carrier or diluent.

37. (Original) A method of making a compound according to claim 1 wherein said method comprises:

(a) reacting a primary amine with 2-fluoro-1-nitrobenzene to produce an amine substituted nitrobenzene;

(b) reducing said amine substituted nitrobenzene obtained in (a) in the presence of hydrogen and a catalyst to produce an amine substituted aniline; and

(c) reacting said amine substituted aniline obtained in step (b), with an aldehyde to produce a substituted benzimidazole of Formula I.

38. (Original) The method according to claim 37, wherein said catalyst is a metal catalyst.

39. (Original) The method according to claim 38, wherein said metal catalyst comprises a metal selected from the group consisting of: Zn, Sn, Fe, Al, Ti and Pd.

40. (Original) The method according to claim 39, wherein said metal catalyst is Pd/C.

41. (Original) The method according to claim 37, wherein the reactions of steps (a) and (b) are carried out for about 14 to about 17 hours.

42. (Original) The method according to claim 37, wherein the reaction of step (c) is carried out for about 45 to about 50 hours.

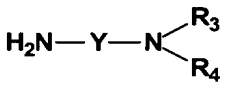
43. (Canceled)

44. (Original) The method according to claim 37, wherein step (b) is carried out in the presence of methanol.

45. (Original) The method according to claim 37, wherein step (c) is carried out in the presence of nitrobenzene and a temperature of about 100 °C.

46. (Currently amended) The method according to claim 37, wherein said primary amine of step (a) is selected from the group consisting of:

(i) an amine of the formula:



wherein

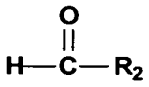
Y is an optionally substituted C_{2-6} alkylene; and

R_3 and R_4 ~~are the same or different and are selected from the group consisting of hydrogen, alkyl, and aryl, or R_3 and R_4~~ together with the nitrogen to which they are attached form a ring having 4 or 5 carbons, which ring optionally contains 1 or 2 additional heteroatoms independently selected from oxygen and NR_5, where R_5 is hydrogen or alkyl, or said ring is optionally substituted with an alkyl or aryl moiety;

~~(ii) pyridylalkyl amine;~~ and

~~(iii)~~ (ii) an optionally substituted piperidin-4-ylalkyl amine, wherein optional substituents are selected from the group consisting of alkyl, aryl and aralkyl.

47. (Original) The method according to claim 37, wherein said aldehyde of step (c) has the formula:



wherein:

R_2 is selected from the group consisting of:

(i) optionally substituted phenoxyphenyl;

(ii) optionally substituted benzyloxyphenyl;

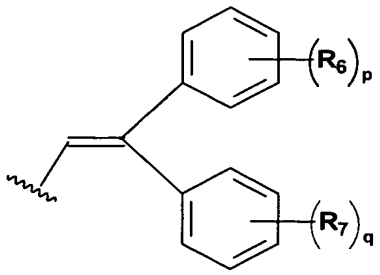
(iii) optionally substituted phenylthiophenyl;

(iv) optionally substituted benzylthiophenyl;

(v) optionally substituted phenylaminophenyl;

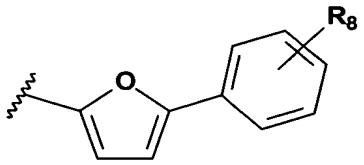
(vi) optionally substituted benzylaminophenyl;

(vii)



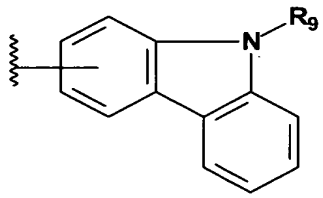
wherein R_6 and R_7 are independently halogen, alkyl, alkoxy or haloalkyl; and p and q are integers from 0 to 4;

(viii)



wherein R_8 is hydrogen, halogen, alkyl or alkoxy;

(ix)



wherein R_9 is hydrogen or alkyl; and

(x) naphthalyl.

48. (Original) The method according to claim 46, wherein said primary amine is 1-(2-aminoethyl)piperidine.

49. (Canceled)

50. (Original) A method of treating, preventing or ameliorating a disorder responsive to blockage of sodium channels in a mammal suffering therefrom, comprising

administering to a mammal in need of such treatment an effective amount of a compound according to claim 1, or pharmaceutically acceptable salt thereof.

51. (Original) The method according to claim 50, wherein said disorder is selected from the group consisting of neuronal damage, a neurodegenerative condition, acute or chronic pain, depression, and diabetic neuropathy.

52. (Original) The method according to claim 51, wherein said neuronal damage is caused by focal or global ischemia.

53. (Original) The method according to claim 51, wherein said neurodegenerative condition is amyotrophic lateral sclerosis (ALS).

54. (Original) The compound according to claim 1, wherein said compound functions as an antitinnitus agent, anticonvulsant, antiarrhythmic, local anesthetic, or antimanic depressant.

Claims 55-59 (Canceled)

60. (Original) A pharmaceutical composition for treatment of a mammal having a disorder or condition responsive to blockage of sodium channels, which comprises an amount of the compound according to claim 1, or a pharmaceutically effective salt thereof, that is effective for treating said disorder or condition, and a pharmaceutically acceptable carrier.

61. (Canceled)

62. (Original) The compound according to claim 1, wherein n is 0.